Meningococcal disease is an acute, potentially severe illness caused by the bacteria *Neisseria meningitidis*. Illness believed to be meningococcal disease was first reported in the sixteenth century. The first definitive description of the disease was by Vieusseux in Switzerland in 1805. The bacteria was first identified in the spinal fluid of patients by Weichselbaum in 1887.

Neisseria meningitidis is a leading cause of bacterial meningitis and sepsis in the United States. It can also cause focal disease, such as pneumonia and arthritis. *N. meningitidis* is also a cause of epidemics of meningitis and bacteremia in sub-Saharan Africa. The World Health Organization estimated meningococcal disease was the cause of 171,000 deaths worldwide in 2000.

The first monovalent (group C) polysaccharide vaccine was licensed in the U.S. in 1974. The current quadrivalent vaccine was licensed in 1978. Meningococcal conjugate vaccine is licensed in Europe, and has had a major impact on the incidence of type C meningococcal disease in the United Kingdom. A meningococcal conjugate vaccine may be available in the United States in the future.

Neisseria meningitidis

- Severe acute bacterial infection
- Cause of meningitis, sepsis, and focal infections
- Epidemic disease in sub-Saharan Africa
- Current polysaccharide vaccine licensed in 1978

NEISSERIA MENINGITIDIS

Neisseria meningitidis, or meningococcus, is an aerobic gram-negative diplococcus, closely related to *Neisseria gonorrhea*, and to several nonpathogenic *Neisseria* species, such as *N. lactamica*. The organism has both an inner (cytoplasmic) and outer membrane, separated by a cell wall. The outer membrane contains several protein structures which enable the bacteria to interact with the host cells, as well as other functions.

The outer membrane is surrounded by a polysaccharide capsule that is necessary for pathogenicity because it helps the bacteria resist phagocytosis and complement-mediated lysis. The outer membrane proteins and the capsular polysaccharide comprise the main surface antigens of the organism.

Meningococci are classified using serological methods based on the structure of the polysaccharide capsule. Thirteen antigenically and chemically distinct polysaccharide capsules have been described. Some strains, often those found to cause asymptomatic nasopharyngeal carriage, are not groupable, and do not have a capsule. Almost all invasive disease is caused by one of five serogroups: A, B, C, Y, and W-135. The relative importance of each serogroup depends on geographic location, as well as other factors, such as age. For instance, serogroup A is a major cause of disease in sub-Saharan Africa, but is rarely isolated in the United States.

Neisseria meningitidis

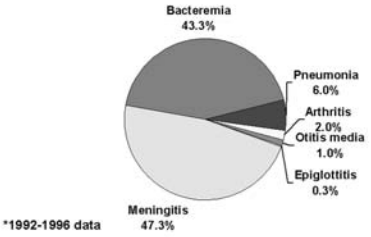
- Aerobic gram-negative bacteria
- At least 13 serogroups based on characteristics of the polysaccharide capsule
- Most invasive disease caused by serogroups A, B, C, Y, and W-135
- Relative importance of serogroups depends on geographic location and other factors (e.g. age)

Meningococci are further classified on the basis of certain outer membrane proteins. Molecular subtyping using specialized laboratory techniques (e.g., pulsed-field electrophoresis) can provide useful epidemiologic information.

Meningococcal Disease
Pathogenesis

- Organism colonizes nasopharynx
- In some persons organism invades bloodstream and causes infection at distant site
- Antecedent URI may be a contributing factor

Neisseria meningitidis
Clinical Manifestations*



Meningococcal Meningitis

- Most common pathologic presentation
- Result of hematogenous dissemination
- Clinical findings
  - –fever
  - – headache
  - –stiff neck

Meningococcemia

- Bloodstream infection
- May occur with or without meningitis
- Clinical findings
  - –fever
  - –petechial/purpuric rash
  - –hypotension
  - –multiorgan failure

PATHOGENESIS

Meningococci are transmitted by droplet aerosol or secretions from the nasopharynx of colonized persons. The bacteria attach to and multiply on the mucosal cells of the nasopharynx. In a small proportion (<1%) of colonized persons the organism penetrates the mucosal cells and enters the bloodstream. The bacteria spread by way of the blood to many organs. In about 50% of bacteremic persons the organism crosses the blood-brain barrier into the cerebrospinal fluid and causes purulent meningitis. An antecedent URI may be a contributing factor.

CLINICAL FEATURES

The **incubation period** of meningococcal disease is 3-4 days, with a range of 2-10 days.

Meningitis is the most common presentation of invasive meningococcal disease and results from hematogenous dissemination of the organism. Meningeal infection is similar to other forms of acute purulent meningitis, with sudden onset of fever, headache, and stiff neck, often accompanied by other symptoms, such as nausea, vomiting, photophobia (eye sensitivity to light), and altered mental status. Meningococci can be isolated from the blood in up to 75% of persons with meningitis.

Meningococcal sepsis (bloodstream infection or meningococcemia) occurs without meningitis in 5%-20% of invasive meningococcal infections. This condition is characterized by abrupt onset of fever and a petechial or purpuric rash, often associated with hypotension, shock, acute adrenal hemorrhage, and multiorgan failure.

Less common presentations of meningococcal disease include pneumonia (5%-15% of cases), arthritis (2%), otitis media (1%), and epiglottitis (<1%).

The **case fatality rate** of invasive meningococcal disease is 9%-12%, even with appropriate antibiotic therapy. The fatality rate of meningococcemia is up to 40%. Up to 20% of survivors have permanent sequelae, such as hearing loss, neurologic damage, or loss of a limb.

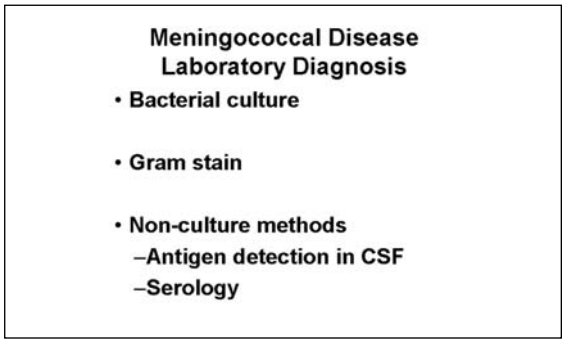
LABORATORY DIAGNOSIS

Invasive meningococcal disease is typically diagnosed by isolation of *N. meningitidis* from a normally sterile site. However, sensitivity of bacterial culture may be low, particularly when performed after initiation of antibiotic therapy. A Gram stain of cerebrospinal fluid showing gram negative diplococci strongly suggests meningococcal meningitis.

Kits to detect polysaccharide antigen in cerebrospinal fluid are

rapid and specific but false negative results are common, particularly in serogroup B disease. Antigen tests of urine or serum are unreliable.

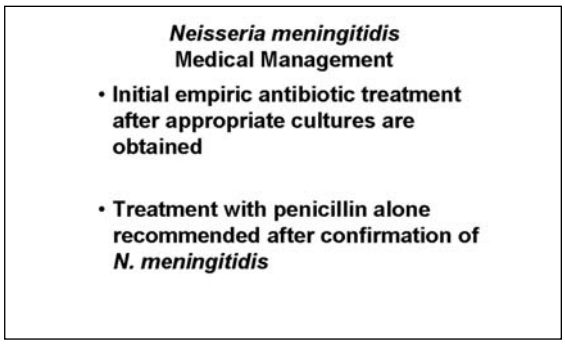
Serologic testing (e.g., enzyme immunoassay) for antibodies to polysaccharide may be used as part of the evaluation if meningococcal disease is suspected but should not be used to establish the diagnosis.



MEDICAL MANAGEMENT

The clinical presentation of meningococcal meningitis is similar to other forms of bacterial meningitis. Consequently, empiric therapy with broad spectrum antibiotics (e.g., third generation cephalosporin, vancomycin) should be started promptly after appropriate cultures have been obtained.

Many antibiotics are effective for *N. meningitidis* infection, including penicillin. Few penicillin-resistant strains of meningococcus have been reported in the United States. Once *N. meningitidis* infection has been confirmed, penicillin alone is recommended.



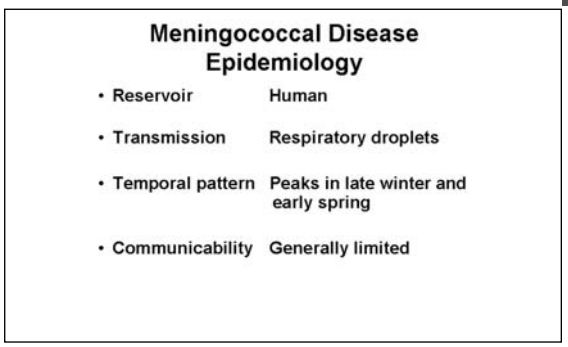
EPIDEMIOLOGY

OCCURRENCE

Meningococcal disease occurs worldwide in both endemic and epidemic form.

RESERVOIR

Humans are the only natural reservoir of meningococcus. Up to 10% of adolescents and adults are asymptomatic transient carriers of *N. meningitidis*, most of which are not pathogenic (i.e, strains that are not groupable).



TRANSMISSION

Primary mode is by respiratory droplet spread or by direct contact.

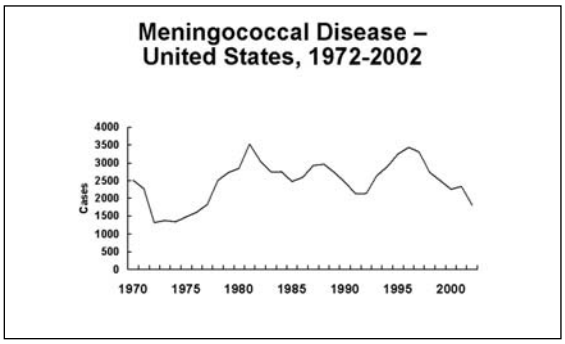
TEMPORAL PATTERN

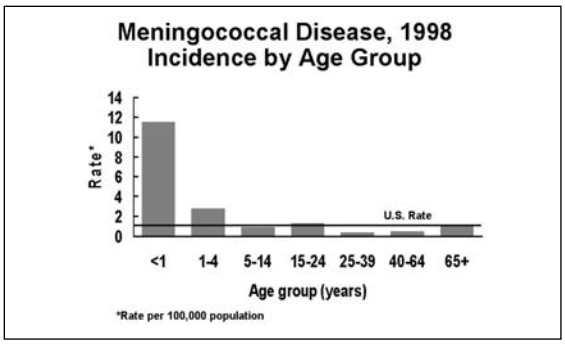
Meningococcal disease occurs throughout the year, However, the incidence is highest in the late winter and early spring.

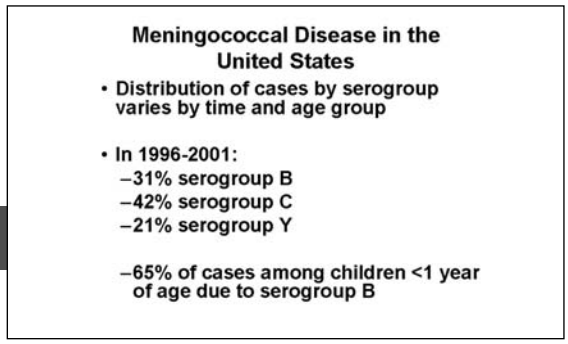
COMMUNICABILITY

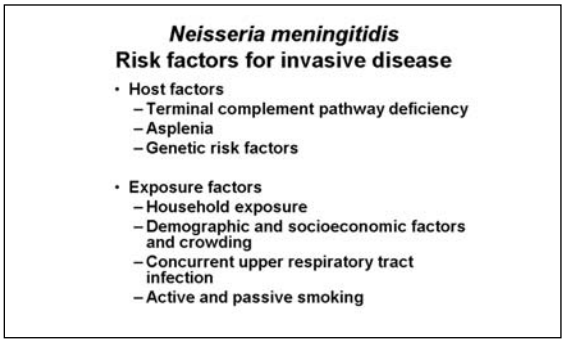
The communicability of *N. meningitidis* is generally limited. In studies of households in which a case of meningococcal disease has occurred, only 3%-4% of households had secondary cases. Most households had only one secondary case. Estimates of the risk of secondary transmission are generally 2-4 per 1000 household

members at risk. However, this risk is 500-800 times that of the general population.









SECULAR TRENDS IN THE UNITED STATES

Approximately 2,500 to 3,000 cases of meningococcal disease are reported each year in the United States (0.8-1.3 cases per 100,000 population). In 2002, an estimated 150 deaths due to meningococcal disease occurred in the United States. **Infants <12 months of age have the highest rates of disease.** Incidence of disease declines in early childhood, increases during adolescence and early adulthood, then declines among older adults. Although incidence is relatively low, more cases occur in persons 23-64 years of age than in any other age group. The proportion of cases among adolescents and young adults has increased in recent years. During 1992-1998, 28% of reported cases were 12-29 years of age.

The proportion of disease caused by different serogroups has changed during the last 15 years. From 1988 to 1991, most cases of meningococcal disease in the United States were due to either serogroup C or B, and serogroup Y accounted for only 2% of cases. However, in 1996-2001, serogroup Y accounted for 21% of cases, with serogroups B and C accounting for 31% and 42%, respectively. Nongroupable strains accounted for 5% of cases. The proportion of cases caused by each serogroup varies by age group. In 2001, 65% of cases among infants aged <1 year were caused by serogroup B, for which no vaccine is available in the United States. Among persons 18-34 years of age, 41% of cases were due to serogroup B, and 25% and 14% were due to serogroups C or Y, respectively.

Risk factors for the development of meningococcal disease include deficiencies in the terminal common complement pathway and functional or anatomic asplenia. Persons with HIV infection are probably at increased risk for meningococcal disease. Certain genetic factors (such as polymorphisms in the genes for mannose-binding lectin and tumor necrosis factor) may also be risk factors.

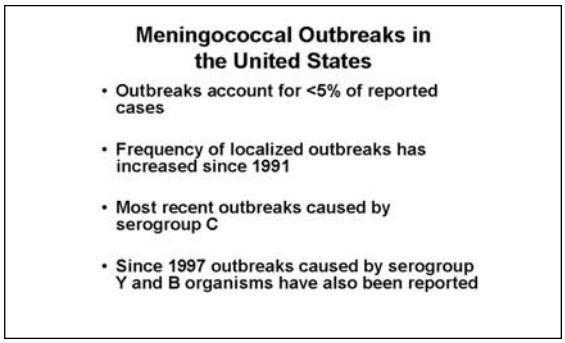
Family members of a person with meningococcal disease are at increased risk. Antecedent viral infection, household crowding, and both active and passive smoking also are associated with increased risk for meningococcal disease. In the United States, blacks and persons of low socioeconomic status have been consistently at higher risk for meningococcal disease. However, race and low socioeconomic status are likely markers for differences in factors such as household crowding, rather than risk factors. During outbreaks, bar or nightclub patronage and alcohol use have also been associated with higher risk for disease.

Cases of invasive meningococcal disease, including at least 2 fatal cases, have been reported among microbiologists. Cases have occurred among persons who work with *N. meningitidis* isolates rather than patient specimens.

Recent studies have shown that college freshmen living in dormitories are at modestly increased risk of meningococcal disease. However, U.S. college students are not at higher risk for meningococcal disease than other people of similar age.

In the United States, **meningococcal outbreaks** account for <5% of reported cases (95%-97% of cases are sporadic). However, since 1991, the frequency of localized outbreaks has increased. Most of these outbreaks have been caused by serogroup C. Since 1997, localized outbreaks caused by serogroup Y and B organisms have also been reported. See http://www.cdc.gov/mmwr/PDF/rr/rr4605.pdf for additional information on the evaluation and management of meningococcal outbreaks.

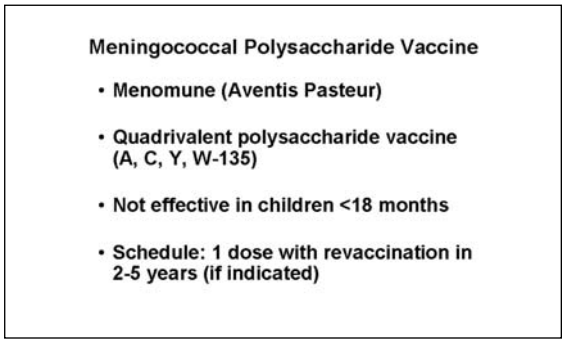
Large outbreaks of serogroup A meningococcal disease occur in the African "meningitis belt", an area that extends from Ethiopia to Senegal. Rates of endemic meningococcal disease in this area are several times higher than in industrialized countries. In addition, outbreaks occur every 8-12 years with attack rates of 500-1000 cases per 100,000 population.



MENINGOCOCCAL POLYSACCHARIDE VACCINE

CHARACTERISTICS

The first meningococcal polysaccharide vaccine (MPV) was licensed in the United States in 1974. The current quadrivalent A, C, Y, W-135 polysaccharide vaccine (Menomune, manufactured by Aventis Pasteur) was licensed in 1978, and is the only formulation currently available in the United States. Each dose consists of 50 µg of each of the four purified bacterial capsular polysaccharides. The vaccine contains lactose as a stabilizer.

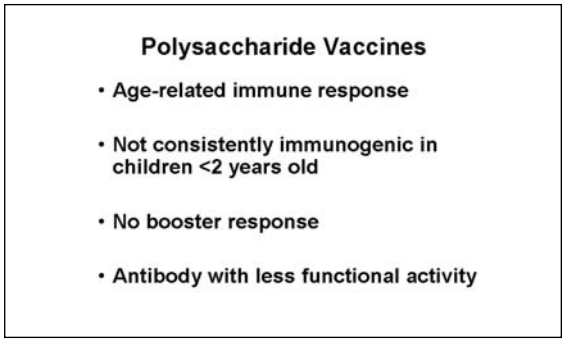


The vaccine is available in single-dose and 10-dose vials. Fifty-dose vials are no longer available. Diluent for the single dose vial is sterile water without preservative. Diluent for the 10-dose vial is sterile water with thimerosal added as a preservative. After reconstitution the vaccine is a clear colorless liquid.

No vaccine is available in the United States for serogroup B.

IMMUNOGENICITY AND VACCINE EFFICACY

The characteristics of MPV are similar to other polysaccharide vaccines (e.g., pneumococcal polysaccharide). The vaccine is not effective among children younger than 18 months of age. The response to the vaccine is typical of a T-independent antigen, with an age-dependent response, and poor immunogenicity in children <2 years of age. In addition, no boost in antibody titer occurs with repeated doses, the antibody which is produced is relatively low-affinity IgM, and "switching" from IgM to IgG production is poor.



Meningococcal Polysaccharide Vaccine Schedule

- Single 0.5-mL dose
- Subcutaneous administration
- Can be administered at the same time as other vaccines
- Protective level of antibody is usually achieved within 7-10 days of vaccination

Meningococcal Polysaccharide Vaccine Recommendations

- Not recommended for routine vaccination of civilians
- Recommended for certain high-risk persons:
  - Terminal complement deficiency
  - Functional or anatomic asplenia
  - Certain laboratory workers
  - Travelers to and U.S. citizens residing in countries in which N. meningiditis is hyperendemic or epidemic (e.g., African meningitis belt)

Meningococcal Endemic Areas 2000

Meningococcal Polysaccharide Vaccine Recommendations

- Control of outbreaks
- Outbreak definition:
  - 3 or more confirmed or probable cases
  - Period <3 months
  - Primary attack rate ≥10 cases per 100,000 population*

*Population-based rates should be used rather than age-specific attack rates

A protective level of antibody is usually achieved within 7-10 days of vaccination. Among infants and children <5 years of age, measurable levels of antibodies against serogroup A and C polysaccharides decrease substantially during the first 3 years following a single dose of vaccine. In healthy adults, antibody levels also decrease, but antibodies are detectable as long as 10 years after vaccination. Although vaccine-induced protection likely persists in school-aged children and adults for at least 3 years, the efficacy of the group A vaccine in children <5 years of age may decrease markedly within this period. In one study, efficacy declined from >90% to <10% three years after vaccination among children who were aged <4 years when vaccinated. Efficacy was 67% among children who were >4 years of age at vaccination.

VACCINATION SCHEDULE AND USE

For both children and adults, MPV is administered **subcutaneously as a single 0.5 mL dose.** The vaccine can be administered at the same time as other vaccines but should be given at a different anatomic site.

Routine vaccination of civilians with MPV is not recommended because of its relative ineffectiveness in children <2 years of age (the age group with the highest risk for sporadic disease) and because of its relatively short duration of protection.

Vaccination with MPV is recommended for certain high-risk groups, including persons who have **terminal complement component deficiencies** and those who have **functional or anatomic asplenia.** Research, industrial, and clinical **laboratory personnel** who are exposed routinely to *N. meningitidis* in solutions that may be aerosolized also should be considered for vaccination. Laboratory workers should also follow appropriate laboratory precautions (biosafety level 2), particularly when working with isolates.

Vaccination with MPV may benefit **travelers to and U.S. citizens residing in countries in which *N. meningitidis* is hyperendemic or epidemic,** particularly if contact with the local population will be prolonged. Recurrent epidemics of meningococcal disease occur in the sub-Saharan Africa "meningitis belt," (Ethiopia in the east to Senegal in the west). Epidemics in the meningitis belt usually occur during the dry season (i.e., from December to June). As a result, vaccination is recommended for travelers visiting the region during this time. Information concerning geographic areas for which vaccination is recommended can be obtained from the CDC Travelers Health website at http://www.cdc.gov/travel/.

Meningococcal polysaccharide vaccine is recommended for use in **control of meningococcal outbreaks.** An outbreak is defined by the occurrence of three or more confirmed or probable cases of meningococcal disease during a period of <3 months, with a resulting primary attack rate of ≥10 cases per 100,000 population.

For calculation of this threshold, population-based rates are used and not age-specific attack rates, as have been calculated for college students. These recommendations are based on experience with serogroup C meningococcal outbreaks, but these principles may be applicable to outbreaks caused by the other vaccine-preventable meningococcal serogroups.

College freshmen, particularly those living in dormitories or residence halls, are at modestly increased risk for meningococcal disease compared with persons the same age who are not attending college. However, **ACIP does not recommend routine MPV vaccination of all college students,** freshmen college students, or students who reside in dormitories. ACIP recommends that providers of medical care to incoming and current college freshmen, particularly those who plan to or already live in dormitories and residence halls, should, during routine medical care, inform these students and their parents about meningococcal disease and the benefits of vaccination. ACIP does not recommend that the level of increased risk among freshmen warrants any specific changes in living situations for freshmen. College freshmen who want to reduce their risk for meningococcal disease should either be administered vaccine by the provider or directed to a site where vaccine is available. Refer to the ACIP statement on this topic at http://www.cdc.gov/mmwr/PDF/rr/rr4907.pdf for more information.

Meningococcal Polysaccharide Vaccine for College Students

- ACIP does not recommend routine vaccination for college students
- Inform students about meningococcal disease and benefits of vaccination
- Administer if requested or direct to site where vaccine is available (e.g., college health service)

REVACCINATION

Revaccination may be indicated for persons at high risk for infection (*e.g.,* persons residing in areas in which disease is epidemic), particularly for children who were first vaccinated when they were <4 years of age. Such children should be considered for revaccination after 2-3 years if they remain at high risk. Although the need for revaccination of older children and adults has not been determined, antibody levels rapidly decline in 2-3 years, and if indications still exist for vaccination, revaccination may be considered 3-5 years after receipt of the first dose.

Meningococcal Polysaccharide Vaccine Revaccination

- Revaccination may be indicated for persons at high risk for infection*
- Consider revaccination of children first vaccinated when they were <4 years of age after 2–3 years if they remain at high risk
- The need for revaccination of older children and adults has not been determined
- If indications still exist for vaccination, revaccination may be considered 3–5 years after first dose

*e.g., persons who reside in areas in which disease is endemic (does not include college settings)

Continued attendance of college, or continued residence in a college dormitory is not an indication for revaccination in the absence of another indication (such as asplenia).

ADVERSE REACTIONS FOLLOWING VACCINATION

Adverse reactions to MPV are generally mild. The most frequent are **local reactions,** such as pain and redness at the injection site. These reactions last for 1-2 days, and occur in 5%-10% of recipients. Systemic reactions, such as headache and malaise are reported in 2%-5% of recipients, and low grade fever occurs in up to 3% of vaccinees. Severe reactions to polysaccharide meningococcal vaccine are uncommon.

Meningococcal Polysaccharide Vaccine Adverse Reactions

- Local reactions (erythema, pain) for 1-2 days
- Low grade fever in <2% of children, less commonly in older persons
- Severe reactions rare

All serious adverse events that occur after receipt of any vaccine should be reported to the Vaccine Adverse Events Reporting System (VAERS). See the VAERS website at http://www.vaers.org

Meningococcal Polysaccharide Vaccine Contraindications and Precautions

- Severe allergic reaction to vaccine component or following prior dose of vaccine
- Moderate or severe acute illness

for information on reporting.

CONTRAINDICATIONS AND PRECAUTIONS TO VACCINATION

A **severe allergic (anaphylactic) reaction** to a vaccine component or following a prior dose of meningococcal polysaccharide vaccine is a contraindication to receipt of further doses. A **moderate or severe acute illness** is reason to defer routine vaccination, but a minor illness is not. Pregnancy, breastfeeding, and immunosuppression are not contraindications to vaccination.

VACCINE STORAGE AND HANDLING

MPV should be shipped in insulated containers to prevent exposure to freezing temperature. Vaccine should be stored at refrigerator temperature (2-8° centigrade [35-46° Fahrenheit]). The vaccine must not be exposed to freezing temperature.

Single dose vials of MPV must be used within 30 minutes of reconstitution. Multidose vials must be discarded 10 days after reconstitution.

SURVEILLANCE AND REPORTING OF MENINGOCOCCAL DISEASE

Invasive meningococcal disease is a reportable condition in most states. All healthcare workers should report any case of invasive meningococcal disease to local and state health departments.

ANTIMICROBIAL CHEMOPROPHYLAXIS

In the United States, the primary means for prevention of sporadic meningococcal disease is antimicrobial chemoprophylaxis of close contacts of infected persons. Close contacts include household members, daycare center contacts, and anyone directly exposed to the patient's oral secretions (e.g., through kissing, mouth-to-mouth resuscitation, endotracheal intubation, or endotracheal tube management). Because the rate of secondary disease for close contacts is highest during the first few days after onset of disease in the index patient, antimicrobial chemoprophylaxis should be administered as soon as possible - ideally within 24 hours after identification of the index patient. Chemoprophylaxis administered >14 days after onset of illness in the index patient is probably of limited or no value. Oropharyngeal or nasopharyngeal cultures are not helpful in determining the need for chemoprophylaxis and may unnecessarily delay institution of this preventive measure.

Rifampin, ciprofloxacin, and ceftriaxone are all 90%-95% effective in reducing nasopharyngeal carriage of *N. meningitidis* and are all acceptable alternatives for chemoprophylaxis. Systemic antimicrobial therapy of meningococcal disease with agents other than ceftriaxone or other third-generation cephalosporins may not reliably

eradicate nasopharyngeal carriage of *N. meningitidis*. If other agents have been used for treatment, the index patient should receive chemoprophylactic antibiotics for eradication of nasopharyngeal carriage before being discharged from the hospital. Information on dosage, duration, and route of administration are available in the meningococcal vaccine ACIP statement at www.cdc.gov/mmwr/PDF/rr/rr4907.pdf.

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